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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,164	04/04/2005	Susanne Binder	34157-707.831	5602

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WILSON, SONSINI, GOODRICH & ROSATI
650 PAGE MILL ROAD
PALO ALTO, CA 94304-1050

EXAMINER	
KIM, TAEYOON	
ART UNIT	PAPER NUMBER
1651	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,164	BINDER ET AL.	
	Examiner	Art Unit	
	TAEYOON KIM	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42,45-49 and 53-61* is/are pending in the application.

4a) Of the above claim(s) *60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42,45-49,53-59 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response filed on 10/23/2009 has been received and entered into the case.

Claims 1-41, 43, 44 and 50-52 have been canceled, claim 60 has been withdrawn from consideration as being drawn to non-elected subject matter, and claims 42, 45-49, 53-59 and 61 have been considered on the merits. All arguments have been fully considered.

Response to Arguments

Applicant's arguments filed 10/23/2009 have been fully considered but they are not persuasive.

Applicant alleged that Young et al. teach a graft comprising various layers – one being a membrane which "acts as an adherent substrate" for a separate layer of cells. This interpretation appears to be from the disclosure of "In particular the composite graft of the invention comprises a layer of connecting cells and a layer of photoreceptors" in the abstract. It is acknowledged that the graft of Young et al. comprises multiple layers including connecting layer, photoreceptor layer, RPE layer and basement membrane layer.

Whether or not the graft of Young et al. has multiple layers of cells, Young et al. clearly teach that there is a RPE layer and a basement membrane layer, which can be Bruch's membrane or amniotic membrane.

The question is whether a person of ordinary skill in the art would grow RPE cells on the membrane layer. Young et al. teach that RPE cells can be harvested as a sheet from donor eye or alternatively, RPE cells can be proliferated in culture and secondarily grown as a monolayer prior to being used as a graft (p.14, lines 12-22). Whether the RPE cells of Young et al. are

directly harvested or proliferated in culture as a monolayer, the monolayer of RPE cells can be cultured on an adherent substrate such as amniotic membrane. Therefore, it is the Examiner's position that monolayer of RPE cells taught by Young et al. placed on the culture substrate (i.e. amniotic membrane) is considered as being continuously grown on the membrane under this condition, and thus meets the limitations of the claimed invention.

Furthermore, since RPE cells can be proliferated in culture and grown as a monolayer as taught by Young et al., it would have been obvious to a person of ordinary skill in the art to grow RPE cells in culture (with or without using the amniotic membrane), and secondarily grow them on the amniotic membrane.

Applicant alleged that Young et al. teach away from growing the necessary intact layer of cells on the membrane layer that is to be a component of the graft referring the teaching of Young et al. that delivery of pigment epithelial cells as a suspension results in uneven distribution and failure to form the necessary intact layer of epithelial cells required for the graft. Applicant concluded that Young et al. not explicitly disclose cells grown on the membrane which is to be grafted, one of ordinary skill in the art, understanding the teachings of Young, would not be inclined to attempt growing the cells to be transplanted directly on the membrane that is to be used in the transplant.

The teaching of Young et al. referring suspension or loose sheets of pigment epithelial cells does not teach away a person of ordinary skill in the art not to grow RPE cells on the membrane. The teaching is actually providing a reason why the basement membrane is required to keep the RPE cells with even distribution for the graft. In fact, Young et al. discussed problems associated with the RPE delivered as a loose sheet or as suspension without any

support (p.4, lines 2-8). Thus, this should be construed as the motivation to use basement membrane to provide a growth substrate for the RPE cells (p.5, lines 21-31), and since the basement membrane provides a growth substrate, a person of ordinary skill in the art would have a motivation to use the substrate for culturing RPE cells prior to transplantation.

With regard to the teaching of Snodderly et al., which was presented to support that RPE cells can be grown at a density of the claimed range, applicant asserted that Snodderly et al. is irrelevant to the currently claimed invention. Again, the teaching of Snodderly et al. is simply for supporting the idea of RPE cells. Applicant further argued that since the current amendment is directed to the human RPE, the supporting evidence of Snodderly et al., which is drawn to RPE of a Rhesus monkey, is immaterial. This argument is not persuasive.

Robb (1985) teaches the cell density of RPE in human eye being not much different from Rhesus monkey taught by Snodderly et al. Robb teaches that RPE cell density in human eye at age 6 is around 20-140 cells/0.01 mm^2 (see Table 1 at p.615), which can be recalculated as 2000 to 14000 cells/mm^2 and 8,000 to 56,000 cells/4 mm^2.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 42, 45-49, 53-59 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Young et al. (of record) in view of Robb (1985; Invest. Ophth. Vis. Sci.),

Grueterich et al. (of record) and Tseng (of record).

Young et al. teach a method and a composite graft for the treatment of conditions associated with photoreceptor loss (e.g. age-related macular degeneration), where the composite graft comprising RPE cells grown on a base membrane such as amniotic membrane (abstract and p.12 lines 2-14). Young et al. also teach other types of cells including precursor to RPE cells (p.5, lines 18-19). Young et al. teach that the graft can be delivered to the subretinal space (p.17, lines 7-8). Young et al. also teach the membrane substrate can also serve as a particularly convenient delivery system for various bioactive agents (pharmaceutically active agents) such as growth factors (p.12, line 18 through p.13, line 3).

Young et al. also teach the RPE cells can be derived from human eye since Young et al. teach that photoreceptor cells (PRCs) can be obtained from donated human eye, and PRCs can be harvested simultaneously with RPE (p.15, lines 1-3 and 11-12). Even if it is considered that Young et al. do not teach that RPE cells are from human origin, it would have been obvious to a person of ordinary skill in the art to try human RPE cells in the graft of Young et al. since the method is intended for human treatment.

Young et al. teach that the RPE cells are delivered as an intact epithelium, an epithelial monolayer with the correct polarity, and RPE cells can be harvested as a sheet from donor eyes or alternatively, RPE cells can be proliferated in culture and secondarily grown as a monolayer (p.14).

Although Young et al. do not particularly teach the concentration of RPE cells being 16,000 – 20,000 per 4 mm^2 of amniotic membrane, this limitation is inherently met by the monolayer of RPE cells grown in culture as taught by Young et al. is considered to encompass

the similar number of cells per 4 mm^2 of amniotic membrane. This is because it is known that the RPE cell density of human eyes is about 2,000 RPE cells/mm^2 up to about 14,000 RPE cells/ mm^2, which can be re-calculated as about 8,000 RPE cells/4 mm^2 up to about 56,000 RPE cells/ 4 mm^2, according to Robb (see Table 1). Therefore, it is considered that the monolayer of RPE cells of Young et al. would have the comparable amount of RPE cells per unit area and thus, meet the limitation.

With regard to the limitation of "human amniotic membrane" in claim 46, Young et al. do not particularly teach the source of the amniotic membrane. However, since Young et al. disclose the base membrane can be autologous to a patient, and it would have been obvious to a person of ordinary skill in the art to use human amniotic membrane for human patients.

With regard to the limitation in claims 57 and 58 drawn to the use of excimer laser, Young et al. do not particularly teach the limitation. However, it would have been obvious to a person of ordinary skill in the art to try excimer laser to trim and/or modify the base membrane suitable for transplantation because the excimer laser ablation technique is well known in the art to cut and reshape variety of tissues and laser treatment is commonly used for eye diseases as numerously disclosed in Young et al. (e.g. p.2, line 18). Since the technique is readily available in the art, and a person of ordinary skill in the art would recognize the technique suitable for modifying amniotic membrane, a person of ordinary skill in the art would choose to use the excimer laser technique in place of the surgical instrument for cutting the substrate for transplantation.

The Supreme Court recently states in KSR v. Teleflex (550 US82 USPQ2d 1385, 2007) "The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim

cannot be proved obvious merely by showing that the combination of elements was "obvious to try." Id., at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103."

The limitation of claim 58 is considered as a result of the method step in claim 57. Claim 58 contains a "wherein" clause that merely states the result of the limitations in the claim and therefore, adds nothing to the patentability or substance of the claim. Therefore, this phrase does not limit the claim. See *Texas Instruments Inc. v. International Trade Commission*, 26 USPQ2d 1010 (Fed. Cir. 1993); *Griffin v. Bertina*, 62 USPQ2d 1431 (Fed. Cir. 2002); *Amazon.com Inc. v. Barnesandnoble.com Inc.,* 57 USPQ2d 1747 (Fed. Cir. 2001).

Young et al. do not teach the amniotic membrane being epithelially denuded.

Grueterich et al. teach the use of epithelially denuded amniotic membrane in culturing limbal epithelium (see whole document; p.64, Materials and Method).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to use epithelially denuded amniotic membrane of Grueterich et al. in the method of Young et al.

The skilled artisan would have been motivated to make such a modification because both intact and epithelially denuded amniotic membrane would be suitable for support of epithelial cell culture. Since amniotic membrane is a suitable substrate for culturing not only corneal

epithelial cells as taught by Grueterich et al. but also for RPE cells, a person of ordinary skill in the art would have considered the choice of intact or denuded amniotic membrane as a routine optimization procedure to obtain optimal environment for culturing RPE cells for treating a retinal disorder.

Although Young et al. do not particularly teach the intact amniotic membrane having a basement membrane and a stroma, Tseng teaches that an amniotic membrane comprises two major components: the basement membrane and stroma (see col. 1, lines 23-24). Therefore, it would have been obvious to a person of ordinary skill in the art that the amniotic membrane of Young et al. inherently comprises basement membrane and stroma.

Young et al. do not teach a step of adding mesenchymal cells to the stroma of the amniotic membrane or the mesenchymal cells being fibroblasts.

Tseng teaches that when fibroblasts (mesenchymal cells) are grown in the stromal side of amniotic membrane, it provides an environment comparable to isolated collagen (fibroblasts are collagen-producing cells) and better cell growth in culture than a plain plastic surface.

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to add fibroblasts on the stromal side of the amniotic membrane of Young et al.

The skilled artisan would have been motivated to make such a modification because Tseng teaches an advantage given by the fibroblast culture on the stromal side of the amniotic membrane providing better cell culture environment for epithelial cells (see col. 4).

With regard to the limitation in claims 57 and 58 drawn to the use of excimer laser, Young et al. do not particularly teach the limitation. However, it would have been obvious to a

person of ordinary skill in the art to try excimer laser to trim and/or modify the base membrane suitable for transplantation because the excimer laser ablation technique is well known in the art as supported by Tseng (e.g. col. 3, line 19) to cut and reshape variety of tissues and laser treatment is commonly used for eye diseases as numerously disclosed in Young et al. (e.g. p.2, line 18). Since the technique is readily available in the art, and a person of ordinary skill in the art would recognize the technique suitable for modifying amniotic membrane, a person of ordinary skill in the art would choose to use the excimer laser technique in place of the surgical instrument for cutting the substrate for transplantation.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAEYOON KIM whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taeyoon Kim/
Primary Examiner, Art Unit 1651